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EPIDEMIOLOGIC STUDIES OF PARKINSON'S DISEASE

III. A COMMUNITY-BASED SURVEY

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Kessler, I. (Johns Hopkins Univ. School of Hygiene and Public Health, Baltimore, Md. 21205). Epidemiologic studies of Parkinson's disease. III. A community-based survey. *Am J Epidemiol* 96: 242–254, 1972.—Community-based samples of patients with and without Parkinson's disease in Baltimore from 1967 to 1969 were obtained through the establishment of a representative panel of 112 physicians. The panel was composed of two subpanels: one consisting of all but two neurologists and neurosurgeons in greater Baltimore ("neurological panel") and the other comprising a stratified sample of other practicing physicians in the area ("nonneurological panel"). Prevalence estimates for Parkinson's Disease in metropolitan Baltimore were generated. The significantly reduced frequency of this condition among Negroes, reported in an earlier hospital-based study, was again observed. The same held for the significantly decreased relative risk of Parkinson's disease among cigarette smokers. Previously noted relationships between parkinsonism and other diseases, such as arteriosclerosis and encephalitis, were verified. When patients referred by neurological and nonneurological panel physicians were compared, their characteristics were generally found to be similar. It was concluded that variability in diagnosis has not substantially affected recent studies on Parkinson's disease.

diseases, related conditions; health surveys; nervous system diseases; neurologic manifestations; Parkinson's disease, prevalence; smoking

Parkinson's disease is consistently and reliably diagnosed in the presence of its classical neurologic triad of tremor, rigidity and hypokinesia. When any of these stigmata are absent, or when they are observed in patients with concomitant unrelated cerebrovascular or neurologic impairments, the diagnosis becomes more tenuous. The degree

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of misclassification probably increases with prevalence of the concomitant conditions, i.e. with age.

In a previously reported investigation (1, 2) *all patients hospitalized over a recent* three-year period in any metropolitan Baltimore hospital with a diagnosis of Parkinson's disease were studied. Comparisons were made with nonparkinsonians who resembled the cases in age, sex, race and date of hospitalization. The referring physicians' diagnoses of parkinsonism were accepted; a review of the clinical records indicated that these diagnoses were valid in 94.7 per cent of the cases.

Hospital-based epidemiologic studies are considered methodologically suspect by some investigators (3, 4) who are concerned with the possible effects of differential hospitalization rates upon observed associations. This helps to explain the appeal of community-based studies in which patients are sampled from the population at large rather than from among the hospitalized. It is often assumed that such studies are less subject to selection biases.

For this reason, among others, a community-based epidemiologic study of Parkinson's disease was undertaken in the Baltimore area. In addition to the use of a general population base, the investigation incorporated another methodologic feature, viz. a comparison of the characteristics of patients diagnosed by neurologists or neurosurgeons with those diagnosed by other physicians. It was hoped that this comparison would shed some light on the effect of diagnostic variability in studies of Parkinson's disease.

Methods

A computer tape listing all private practitioners of medicine in the Baltimore area was obtained from commercial sources. The names of physicians specializing in anesthesiology, gynecology, obstetrics, ophthalmology, pathology, pediatrics and psychiatry (except neuropsychiatry) were removed. The remaining names were arranged in random order and stratified into five categories according to type of practice, viz. neurology and neurosurgery, general practice, internal medicine, general surgery, and all other specialties combined.

A stratified random sample of 114, or about 6 per cent, of these physicians was obtained by selecting a predetermined number from each stratum. The sample, comprising a "Physicians Panel for the Study of Parkinson's Disease," was personally approached and asked to identify and enroll in the study all Parkinson's disease patients seen between 1967 and 1969. For analytical purposes the physicians panel was divided into two subpanels: one consisting of all but two neurologists and neurosurgeons in the metropolitan Baltimore area ("neurological panel") and the other comprising a stratified sample of other practicing physicians in the area ("nonneurological panel"). To the neurological panel patients were added 29

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TABLE 1

Physicians sampled and patients referred in the community-based survey

Baltimore area physicians*		Physicians sampled		Patients referred†	
Type of practice	Total No.	No.	% of total	Cases	Controls
Sampled practices:					
Neurology/Neurosurgery	30	28‡	93.3	127	127
General practice	476	31	6.5	55	55
Internal medicine	271	29	10.7	21	21
General surgery	225	6	2.7	3	3
Other	271	18	6.6	22	22
Total	1,273	112	8.8	228	228
Nonsampled practices	619§				
Total, all practices	1,892	112	5.9	228	228

* Excludes physicians without primary responsibility for adult patients.

† Excludes 9 cases and 16 controls who refused to be interviewed.

‡ Two neurosurgeons declined to participate.

§ Anesthesiology, gynecology, obstetrics, ophthalmology, pathology, pediatrics and psychiatry.

parkinsonians seen during the study interval at the Neurology Clinic of the Johns Hopkins Hospital. Except for the two neurologists noted above, all the physicians solicited agreed to participate. Regular and frequent contact was made with all participating physicians throughout the field phases of the study—from late 1968 to early 1970.

Four eligibility criteria were imposed on all cases, viz. that they 1) were alive; 2) were able to communicate intelligibly; 3) resided in greater Baltimore; and 4) were not hospitalized in Baltimore for any reason between 1967 and 1969. The latter criterion assured the exclusion of those patients who had been studied in the earlier, hospital-based, survey. Only nine (or 4 per cent) of the eligible parkinsonians and 16 (or 7 per cent) of the eligible controls refused to participate.

Panel physicians were requested to select as a control the next patient seen after a case who was of the same race, sex and age (within five years) but who did not have Parkinson's disease. The distribution of panel physicians by type of practice and number of patients referred for study is shown in table 1. Five, or 6.0 per cent, of the nonneurologists sampled were Negroes; all of these were general practitioners. They comprised approximately 5.3 per cent of the total number of eligible Negro physicians in the Baltimore area.

In referring parkinsonians for study, the panel physicians submitted, in addition to identifying and demographic data, information on the presence or absence of specific neurologic signs as well as on the use of anti-Parkinson medications. For control patients, only identifying and demographic data were obtained.

All patients were interviewed at home by trained personnel who were not informed as to the case or control status of each respondent. However, because the interviewers knew that parkinsonian patients were included in the survey, they were asked to note the precise point in the interview at which they suspected any respondent to have Parkinson's disease.

Every fifth completed interview was validated by the supervising interviewer who telephoned the specified patient and did the following: 1) confirmed that the interview had been made; 2) ascertained the date and duration of the interview; 3) repeated the questions on smoking history; 4) repeated the question on encephalitis; and 5) inquired as to whether any problems had arisen during the interview. All interviews were found, in fact, to have taken place and no substantial changes in responses on smoking or encephalitis were noted.

In the analysis of the findings, χ^2, *t*- and *z*-tests, confidence intervals for normal and Poisson distributions as well as relative risk statements were employed to assess the significance of differences between Parkinson's disease patients and controls. Group, rather than matched pair, comparisons were made; accordingly the inferences drawn are conservative, i.e. less likely to have attained statistically significant values. The "direct" method of age standardization was used in comparing various characteristics of the

neurologists' and neurosurgeons' cases with those of the other panel physicians.

Findings

Of the 127 parkinsonians referred by the neurologists and neurosurgeons ("neurological panel") 71, or 55.9 per cent, were males and 56 (44.1 per cent) were females. Among the 101 cases identified by the other physicians ("nonneurological panel"), 51 were males and 50 were females. There were 28 cases under 55 years of age, all but three of whom were referred by the neurological panal (table 2). This reflects the significantly younger ($p < .025$) age distribution of the neurological panel patients as compared with the nonneurological panel patients.

Only 17, or 7.5 per cent, of the parkinsonians (12 males and five females) were nonwhite; all of these were Negro and 55 years of age or older. Eight of these were patients at the Johns Hopkins Neurology Clinic, while four were private patients of the neurological panel. Of the five remaining nonneurological panel cases, three were patients of Negro general practitioners and two were referred by other white physicians. Negroes represented 9.4 per cent of neurological panel patients and 5.0 per cent of nonneurological panel patients.

As calculated from age-grouped data, the mean ages of the Negro patients were 72.5 years for males and 66.0 years for females; among whites, the corresponding figures were 65.2 years and 67.5 years, respectively.

The diagnosis of Parkinson's disease was received by 131 (57.5 per cent) of the cases five years or less prior to the study. Patients from the two panels did not differ significantly in this respect. Neurologic symptoms, as anticipated, tended to precede

Table 2

*Distribution of cases and controls by age and physician panel**

Age (years)	Cases			Controls		
	Neuro†	Other‡	Total	Neuro†	Other‡	Total
Males						
<45	6 (8.5)	0	6 (4.9)	4 (5.6)	0	4 (3.3)
45-54	10 (14.1)	1 (2.0)	11 (9.0)	12 (16.9)	4 (7.8)	16 (13.1)
55-64	26 (36.6)	11 (21.6)	37 (30.3)	24 (33.8)	13 (25.5)	37 (30.3)
65-74	16 (22.5)	24 (47.1)	40 (32.8)	27 (38.0)	22 (43.1)	49 (40.2)
75-84	13 (18.3)	15 (29.4)	28 (23.0)	4 (5.6)	11 (21.6)	15 (12.3)
85+	0	0	0	0	1 (2.0)	1 (0.8)
All ages	71 (100.0)	51 (100.0)	122 (100.0)	71 (100.0)	51 (100.0)	122 (100.0)
Females						
<45	0	0	0	0	1 (2.0)	1 (0.9)
45-54	9 (16.1)	2 (4.0)	11 (10.4)	7 (12.5)	1 (2.0)	8 (7.5)
55-64	21 (37.5)	9 (18.0)	30 (28.3)	24 (42.9)	13 (26.0)	37 (34.9)
65-74	20 (35.7)	23 (46.0)	43 (40.6)	23 (41.1)	18 (36.0)	41 (38.7)
75-84	6 (10.7)	13 (26.0)	19 (17.9)	2 (3.6)	16 (32.0)	18 (17.0)
85+	0	3 (6.0)	3 (2.8)	0	1 (2.0)	1 (0.9)
All ages	56 (100.0)	50 (100.0)	106 (100.0)	56 (100.0)	50 (100.0)	106 (100.0)

* Percentages in parentheses.
† Patients of neurological panel physicians.
‡ Patients of nonneurological panel physicians.

TABLE 3

Estimated prevalence (per 100,000) of Parkinson's disease: metropolitan Baltimore, 1967–1969

Age (years)	Race	No. Cases*	Prevalence†	95% confidence interval‡
Males				
<45	White	22.2	4.10	2.58– 6.19
	Negro			
45–54	White	43.3	44.13	31.73– 59.58
	Negro			
55–64	White	222.3	313.66	273.20– 359.77
	Negro	3.2	19.61	4.29– 55.89
65+	White	698.2	1,224.05	1,135.92–1,319.53
	Negro	68.5	545.17	426.87– 692.37
All ages	White	966.1	128.37	120.54– 136.71
	Negro	71.7	30.66	24.13– 38.94
Females				
<45	White			
	Negro			
45–54	White	54.8	52.69	39.78– 69.02
	Negro	1.1	4.17	0.15– 22.39
55–64	White	171.8	223.43	191.93– 259.85
	Negro	2.1	11.78	1.53– 41.70
65+	White	746.7	852.62	792.94– 916.57
	Negro	19.9	118.28	71.20– 184.52
All ages	White	897.1	121.47	113.94– 129.37
	Negro	14.7	8.67	5.45– 13.09

* Estimated by applying the inverse of the physician sampling fractions to the number of cases referred by the neurological and nonneurological panels. Included in the latter were 46 otherwise eligible cases (20 white males, 19 white females, 4 Negro males and 4 Negro females) who were not interviewed, primarily because they had been included in the hospital survey.

† Calculated on the basis of the 1970 U.S. Census population estimates for the Baltimore Standard Metropolitan Statistical Area.

‡ Estimated as Poisson variate.

the diagnosis date—by up to a year in 28.6 per cent, two to five years in 31.0 per cent and six to 10 years in 6.9 per cent. The median age at diagnosis in neurological panel patients was 60.3 years and 61.3 years in males and females, respectively; in nonneurological panel patients the corresponding ages were 65.8 and 68.1 years.

Thirteen of the cases were first diagnosed below the age of 40. Four of these were attributed to anticedent encephalitis, four were termed "idiopathic" and the remainder were indeterminate as to cause. Only one case occurred in an individual born after 1930, and this was considered to be the "idiopathic" variety. Ten of these cases were identified by the neurological panel and three by the nonneurological panel.

The prevalence of Parkinson's disease in metropolitan Baltimore between 1967 and 1969 was estimated from the total number of cases referred by the sampled physicians, including the nine nonrespondents as well as 37 otherwise eligible patients who were not interviewed, primarily because of their inclusion in the earlier hospital-based survey. The total number of cases referred by each panel, neurological and nonneurological, was multiplied by the inverse of the respective physician sampling fractions (cf. table 1). The resulting numbers of cases were converted to rates by dividing them by the estimated Baltimore area populations of given age, sex and race obtained from the 1970 census (5).

The estimated prevalence rates for Parkinson's disease in metropolitan Baltimore show a marked increase with age and a modest predilection for males over females in both races above 54 years of age (table 3). Prevalence among Negroes was invariably and significantly lower than among whites in each age and sex category. The apparent deficit of Negro cases was especially remarkable for the females, in which a 14-fold overall discrepancy between the races was evident.

At the time of the study, 160 or 70.2 per cent of the cases were currently taking one or more anti-Parkinson drugs. The proportions, by type of physician, were 75.6 per cent for neurological panel patients and 63.4 per cent for nonneurological panel patients ($p < .05$). Eleven cases (4.8 per cent) were receiving L-dihydroxyphenylalanine (L-dopa), all under the supervision of a neurologist or neurosurgeon. There were no substantial differences between the sexes or between age groups in the use of drug therapy. A significantly higher percentage of neurological panel patients (18.1 per cent) than nonneurological

panel patients (8.9 per cent) had undergone surgical intervention for their disease ($p < .05$).

Panel physicians reported on the presence or absence of four neurologic signs: tremor, rigidity, slowness and abnormalities of facies. With two exceptions, the proportion of patients from each panel with abnormal signs was greater, though not significantly so, in males as compared with females (table 4). Tremor and facial abnormalities were more prevalent among female nonneurological panel patients but these differences were also not statistically significant. Cases from the two panels did not differ in the duration of their neurologic signs at the time of interview. Separate comparisons by race were not made because of the small number of Negro patients.

Cases and controls were questioned directly about a number of neurologic symptoms, including those reported by the panel physicians. As expected, the neurologic symptoms were significantly more prevalent among the cases from each panel as compared with the controls ($p < .05$). It should be noted that neurologic signs observed by physicians are not strictly comparable to symptoms reported by patients.

In general, neurological panel patients tended to report these symptoms more frequently than did nonneurological panel patients. This was true in both sexes with regard to slow starts, loss of arm swing, trouble with speech, trouble walking, nervousness, trouble with memory, excessive yawns or hiccoughs and paralysis. Among female cases, those referred by the neurological panel were more likely than nonneurological panel patients to report tremor, trouble using hands, change in posture and facial changes. Among male cases, stiffness was more prevalent in patients from the neurological panel. The magnitude of these differences between the panels, which were age-adjusted, was generally rather small. Statistical significance was obtained only for slow starts, loss of arm swing, change in posture and facial changes among female cases from the neurological and nonneurological panels.

TABLE 4

Proportion of parkinsonians with abnormal neurologic signs

Sign	Sex	% Neurological panel patients	% Nonneurological panel patients*	z-value†	p
Tremor	Male	73.2	74.2	0.12	>0.80
	Female	71.4	89.0	2.25	<0.03
Rigidity	Male	73.2	61.3	1.05	>0.20
	Female	58.9	53.0	0.61	>0.40
Slowness	Male	67.6	73.3	0.68	>0.40
	Female	53.6	59.3	0.59	>0.50
Facies	Male	57.7	45.2	1.35	>0.10
	Female	50.0	60.0	1.03	>0.20

* Percentages adjusted to age distribution of the neurological panel patients.

† For two-tailed differences in proportions between patients from the two panels.

Neurologic symptoms among control patients of each sex were more common in the neurological panel than in the nonneurological panel, often significantly so. As indicated above, however, symptom prevalence was almost invariably greater among parkinsonians than controls from each panel.

The lay interviewers conducted their interviews blindly; however, they observed neurologic abnormalities in the cases with a much greater frequency than in the controls. Tremor and abnormalities of face, voice, posture and starting of movements were noted by them significantly more often among the parkinsonians ($p < .01$). Cases from the neurological and nonneurological panels were equally likely to have their neurologic signs detected by the interviewers. As was true for the physician-reported signs, a greater frequency of neurologic abnormalities was noted by the interviewers among neurological panel controls than among controls from the nonneurological panel. These differences attained statistical significance only for tremor in females and for abnormal starting of movements in controls of both sexes ($p < .05$).

Each interviewer was instructed to indi-

cate whether and, if so, when she came to suspect that a particular patient had Parkinson's disease or any other neurologic disorder. Twenty-three control patients (10.1 per cent) and 187 parkinsonians (82.0 per cent) were suspected, about one-half of them in the early phases of the interview. Female cases referred by nonneurologists were suspected somewhat less frequently (66 per cent) than males and neurological panel cases of both sexes (about 88 per cent). Controls referred by the neurological panel tended to be suspected of parkinsonism (or other neurologic disorder) more frequently (15.0 per cent) than the nonneurological controls (4.0 per cent).

All patients were queried in detail on their history of selected prior illnesses. In general, the spectrum of disease was similar in cases and controls, whether examined in toto or separately by type of physician panel. Relative risks of only three conditions were significantly elevated among parkinsonians: encephalitis (or Spanish flu) in females and "hardening of the arteries" and prostate disorders in males. Heart disease, stroke and peptic ulcer were reported significantly less often by male cases, and diabetes by female cases. Though the figures do not attain statistical significance, arteriosclerosis was considerably more prevalent among parkinsonians than controls (table 5).

Time relationships between the prior illnesses and Parkinson's disease in the two patient panels were also scrutinized. There were no significant differences in these relationships for encephalitis/Spanish flu, arteriosclerosis, head injuries, stroke or psychiatric disorders between the neurological and nonneurological panel cases.

The four childhood exanthematous viral diseases (chicken pox, measles, German measles and mumps) were somewhat less frequent in male cases than controls, and there were no differences in the reported prevalence of cancer or "tumors." The relative risk of head injuries was moderately increased in female cases and reduced in males; the reverse pattern obtained for allergies.

All patients were questioned in detail on their exposure to a variety of possible risk factors in the pathogenesis of Parkinson's disease. These included contacts with animals, medications taken, condition at birth and smoking habit. Cases and controls did not differ significantly in the degree of their exposure to dogs, cats, birds, other pets or other animals. No differences in the use of tranquillizers, drugs for sleeping, blood pressure control, allergies, weight loss or other purposes could be discerned. Only four cases and two controls reported that their condition at birth, for any reason, was not good. These numbers are too small to permit generalization.

A thorough smoking history was obtained from all patients. Among males, the proportion of cases who ever (more than trivially) smoked cigarettes (45.9 per cent) was significantly smaller ($p < .001$) than the proportion of controls (68.9 per cent) (table 6). Relatively few women in both categories smoked but, again, there were fewer among cases than controls ($p > .05$). Neurological panel patients in general were more likely than nonneurological panel patients to have smoked. However, within each panel, a significantly smaller proportion of parkinsonians than controls had smoked ($p < .05$). The risk of Parkinson's disease among male smokers was 38 per cent of that observed among nonsmokers, as approximated by the odds ratio. The relative risks for males in the neurological and nonneurological panels were 43 per cent and 32 per cent, respectively. Among female smokers, the corresponding relative risks were 56 per cent for the combined patients, and 50 per cent and 44 per cent for patients in the two individual panels.

Among both males and females who ever smoked, cases did not differ significantly from controls in the age at which cigarette smoking was started. However, the parkinsonian smokers tended to smoke a smaller number of cigarettes than the controls. In

TABLE 5

Reported illnesses: prevalence and relative risk

Illness	Males			Females		
	% Cases	% Controls	Relative risk	% Cases	% Controls	Relative risk
Viral/Bacterial:						
Chicken pox	41.0	46.7	0.79	58.5	49.1	1.46
Measles	62.3	66.4	0.84	71.7	70.8	1.04
German measles	11.5	12.3	0.93	23.6	17.9	1.42
Mumps	46.7	53.3	0.77	54.7	51.9	1.12
Encephalitis/Spanish flu	17.2	12.3	1.48	36.8	12.3	4.15*
Shingles	13.9	9.0	1.63	11.3	12.3	0.91
Heart/Circulatory:						
Heart disease	11.5	32.8	0.27*	21.7	21.7	1.00
Rheumatic fever/heart	0	2.5		3.8	0.9	4.35
Hardening of arteries	18.0	8.2	2.46*	10.4	10.4	1.00
Arteriosclerosis	5.7	1.6	3.72	3.8	2.8	1.37
Stroke	5.7	16.4	0.31*	5.7	9.4	0.58
High blood pressure	21.3	23.0	0.91	28.3	38.7	0.63
Allergic:						
Hay/rose fever	9.0	6.6	1.40	5.7	5.7	1.00
Allergy	17.2	13.1	1.38	16.0	19.8	0.77
Asthma	5.7	7.0	0.80	3.8	4.7	0.80
Neoplastic:						
Cancer	1.6	1.6	1.00	2.8	4.7	0.58
Tumor	9.8	9.0	1.10	27.4	29.2	0.92
Leukemia	0	0		0	0	
Other:						
Diabetes	9.8	11.5	0.84	4.7	14.2	0.30*
Rheumatism/arthritis	28.7	37.7	0.67	53.8	54.7	0.96
Peptic ulcer	11.5	21.3	0.48*	6.6	14.2	0.43
Nervous breakdown	4.1	9.8	0.39	5.7	7.5	0.75
Other mental illness	0.8	0.8	1.00	2.8	0	
Head injury	18.0	23.8	0.70	16.0	10.4	1.64
Prostate	29.5	17.2	2.01*	0	0	
Menstrual trouble				29.2	31.1	0.91
Other illnesses	32.0	40.2	0.70	36.8	35.0	1.08

* Prevalence of illness significantly different in cases and controls at 95% confidence level.

males, the difference was of marginal statistical significance ($p \sim .05$); in females it was not significant. These smoking patterns obtained both in the recent and in the remote past of each respondent.

A smaller proportion of male cases (76.8 per cent) than controls (88.1 per cent) who smoked reported inhaling; among females the corresponding figures were 65.4 per cent and 76.9 per cent ($p > .05$). The mean duration of cigarette smoking tended to increase with age and was longer in males than females. On the average, male cases had smoked 1.2 years less than male controls; among females, the mean difference was 5.4 years. Neither of these differences attained statistical significance, however.

Although filter-tip cigarettes were used more commonly by case and control females, there were no significant differences in this practice between parkinsonians and controls of either sex. Relatively more patients with Parkinson's disease than controls had stopped smoking: among males, 57.1 vs. 52.4 per cent and among females, 50.0 vs. 41.0 per cent ($p > .30$). Somewhat

TABLE 6

*Number of patients who ever smoked cigarettes**

Age (years)	Males		Females	
	Cases	Controls	Cases	Controls
<45	4 (66.7)	3 (75.0)	0	1 (100.0)
45–54	8 (72.7)	13 (81.3)	5 (45.5)	4 (50.0)
55–64	19 (51.4)	28 (75.7)	7 (23.3)	20 (54.1)
65–74	17 (42.5)	29 (50.1)	11 (25.6)	12 (30.3)
75+	8 (28.6)	11 (73.3)	3 (15.8)	2 (11.1)
Total: All ages†	56 (45.9)	84 (68.9)	26 (24.5)	39 (36.8)

* Percentages in parentheses.

† In males, χ^2 (1 d.f.) = 12.22, $p < .001$. In females, χ^2 (1 d.f.) = 3.20, $p > .05$.

TABLE 7

Mean age at onset of neurologic symptoms reported by cases who ever smoked or never smoked cigarettes

Neurologic symptoms	Sex	Ever smoked	No. of cases	Mean age (years)	95% confidence interval* (years)
Tremor	Male	Yes	51	57.4	± 3.18
		No	56	60.9	± 2.98
	Female	Yes	24	57.1	± 5.08
		No	72	58.6	± 3.41
Rigidity	Male	Yes	33	56.2	± 3.98
		No	38	59.7	± 3.45
	Female	Yes	11	55.9	± 8.71
		No	45	60.0	± 4.25
Hypokinesia	Male	Yes	38	59.7	± 3.90
		No	42	62.4	± 3.78
	Female	Yes	10	66.0	± 7.10
		No	53	62.2	± 3.35
Facies	Male	Yes	19	58.7	± 5.84
		No	18	60.6	± 6.88
	Female	Yes	7	62.1	± 8.82
		No	20	59.2	± 5.37
Speech	Male	Yes	27	58.3	± 3.96
		No	36	62.2	± 4.86
	Female	Yes	12	61.7	± 7.33
		No	31	59.8	± 6.12

* Calculated as $t_{.05}S_{\bar{x}}$, where $t_{.05}$ is the appropriate value for the degrees of freedom involved and where $S_{\bar{x}}$ is the standard error about the mean.

fewer than half of the cases who stopped smoking did so for reasons of health (males, 46.9 per cent; females, 38.5 per cent). This was true for about two-thirds of the corresponding controls (males, 72.7 per cent; females, 62.5 per cent). None of the above comparisons on cigarette smoking revealed any substantial differences in smoking characteristics between neurological panel and nonneurological panel patients.

All patients were queried in detail concerning symptoms relating to neurologic deficits such as tremor, rigidity, hypokinesia, facies and speech. The parkinsonians were classified into those who were (or had been) cigarette smokers and those who were (or had) not. After adjusting for group differences in age distribution, it was found that a significantly smaller ($p < .01$) proportion of female case smokers (38.5 per cent) than nonsmokers (68.1 per cent) reported having symptoms attributable to hypokinesia. For no other neurologic deficits were there any statistically significant differences between smokers and nonsmokers. However, the prevalence of all five deficits was diminished in female parkinsonians who smoked, relatively more so among those from the neurological panel than from the nonneurological panel. No consistent pattern was evident among the male cases.

The neurologic symptoms tended to appear at an earlier age among the parkinsonians who had smoked cigarettes as compared with those who had not (table 7). In males, the mean age at symptom onset was invariably younger in the smokers than in the nonsmokers, the mean difference for all symptoms being 3.1 years. This pattern was observed only for tremor and rigidity in female cases, but the number of female smokers with the remaining symptoms was quite small. Similar relationships held for both neurologic and nonneurologic patients of both sexes. None of the observed age differences were statistically significant, however.

It has been previously suggested (1) that, to some extent, the above relationships may reflect the somewhat younger mean ages of the smokers as compared with the nonsmokers. Among male cases, the mean ages

at the time of study were 63.0 and 68.3 years in smokers and nonsmokers, respectively; among females, the corresponding ages were 64.6 and 68.4 years.

The findings on cigar and pipe smoking habits among male cases and controls were not entirely consistent with those on cigarette smoking. The parkinsonians (34.4 per cent) were more likely to have smoked cigars than the controls (25.4 per cent) ($p > .10$); pipe smoking was nearly equal in frequency among both groups (22.1 and 23.8 per cent, respectively). The relative risk of Parkinson's disease among cigar smokers was 1.54; for pipe smokers it was 0.91. Of those smoking, only 9.5 per cent of the cases and 22.6 per cent of the controls regularly smoked less than one cigar per day ($p > .10$). Among pipe smokers the proportions smoking less than one pipeful per day were 3.7 per cent for cases and 13.8 per cent for controls ($p > .15$). The cases also tended to have begun smoking earlier: 31.0 per cent of the cigar smoking cases and 22.6 per cent of the controls began under 20 years of age ($p > .40$). For pipe smoking the proportions were 37.0 per cent and 24.1 per cent, respectively ($p > .30$). A total of only 11 cases and 16 controls had stopped smoking cigars or pipes for reasons of health. In all of the above comparisons, there were no important differences between neurological panel and nonneurological panel patients.

Cases and controls were also compared in relation to various demographic, anthropomorphic and social characteristics. The two groups resembled each other very closely in marital status, religion, consanguinity, height, weight, and drinking habits. However, cases were somewhat less likely than controls to have been born in Baltimore or Maryland ($p \sim .05$). A significantly greater proportion of the male cases (49 per cent) than controls (35 per cent) were first-generation Americans ($p < .05$) and relatively more of them (50.8 vs. 41.8 per cent) had had more than an eighth grade education ($p > .15$).

Discussion

The principle findings of this community-based survey are in accord with those of the previously reported hospital-based study (1, 2). Parkinson's disease increases markedly with age and is somewhat more prevalent among men than women. Its frequency is unusually low among Negroes of both sexes and all ages. The possible significance of the latter observation, now supported by a study free of possible hospital selection bias, has already been considered (2). Further studies on racial differences in the incidence and clinical manifestations of parkinsonism are indicated.

There have been relatively few attempts to estimate the incidence or prevalence of Parkinson's disease in general populations (6). Brewis et al. (7) surveyed selected neurologic diseases in Carlisle, England, utilizing hospital and physician records. They estimated the point prevalence of parkinsonism on January 1, 1961 to be 112.5 per 100,000 persons. The point prevalence of this disease on January 1, 1955 in Rochester, Minnesota, was calculated by Kurland (8) to be 187 per 100,000. When these rates are directly adjusted to the age distribution of the 1950 United States population, they become 88.1 and 157.0 per 100,000, respectively (7).

The estimated prevalence (1967–1969) of Parkinson's disease among whites in the present survey, when adjusted to the above standard, is 112.2. The similarity and magnitude of these prevalence estimates suggest that they may encompass the true range. Extrapolation to the United States population of approximately 200,000,000 in 1972 yields a minimum estimate of 176,200 and a maximum of 314,000 persons who are afflicted with Parkinson's disease. These figures are consistent with Kurland's calculation of 266,000 cases (8), but not with Doshay's figure of about a million (9). They are not greatly affected by changes in the age composition of the United States since 1950.

In considering the degree to which our prevalence estimates are valid, two potential sources of error are apparent. First, the patient listings provided by the panel physicians might not have been complete. To encourage full participation, the author met in person with each physician and made liberal use of telephone and post. His assistants maintained contact with the physicians' offices on the average of once each week. Panel physicians were encouraged to submit the names of *all* patients, even those whom they did not wish to be interviewed. Twenty-eight names were provided by more than one physician. Nearly all parkinsonians included in the hospital survey who were seen by a panel physician and who would otherwise have been eligible for inclusion in the community survey were, in fact, identified.

The second potential source of error in the prevalence estimates lies in the fact that no special effort was made to include patients seen at two sizable hospital neurology clinics, both university-affiliated, in Baltimore. This proved necessary due to the unavailability of diagnostic registers in the two clinics. However, the number of clinic patients actually excluded from the prevalence figures was probably very small because most of the clinic physicians were neurologists already participating as panel members. At the larger of the two clinics, for example, it is estimated that no more than seven parkinsonians were missed. In view of the above, we consider it likely that the calculated prevalence figures represent a slight underestimation of the actual rates.

The increased relative risks among the sampled parkinsonians of arteriosclerosis (10) and encephalitis (11) were expected; the infrequency of stroke was not. However, closer examination of the data revealed that the apparent inconsistency was limited to neurological panel patients, among whom there were a number of control patients with cerebrovascular disease. In contrast to this, the relative risk of stroke among nonneurological panel cases was exactly 1.00 in both males and females.

The reduced prevalence of heart disease among parkinsonian males was noted in patient groups from both panels as well as in the earlier hospital-based survey. A complete explanation is not readily apparent, in view of the obviously different selective factors operating among the three groups studied. To some extent, however, this may be attributable to the diminished smoking of parkinsonians. The same may apply to the possible reduced risk of peptic ulcer in patients with Parkinson's disease.

The considerably reduced relative risks of the childhood exanthematous viral diseases which were noted among the hospitalized parkinsonians (2) were less apparent in this community-based survey. Risks remained low, albeit less so, among male cases but not among female. The extent to which this discrepancy is due to the smaller sample size of the present study or to the absence of a true (negative) association may be determined in future studies.

No additional light was shed by the present survey on the cancer risks of patients with Parkinson's disease. The number of patients studied was obviously too small to permit any confirmation of the previously reported diminution in such risks (2).

The smoking characteristics of parkinsonians, previously reported for hospitalized cases (1), were observed anew in the community-based sample. Patients destined to develop Parkinson's disease appear less likely to become cigarette smokers. If they do smoke, they tend to smoke fewer cigarettes and over a shorter period of time. They also are less likely to inhale and more likely to stop smoking for any reason. There is some indication that the neurologic concomitants of parkinsonism tend to become manifest at an earlier age among smokers as compared with nonsmokers. However, the possible significance of the latter finding was confounded by the younger mean ages of the smokers relative

to those of the nonsmokers of each sex in this investigation.

The proportions of male and female controls who smoked were nearly identical to those of the Baltimore general population sample who were initially interviewed by the Commission on Chronic Illness in 1953–1954 and reinterviewed in 1966–1967. Thus, it is extremely unlikely that the relationships observed in the community survey were due to the selection of a control sample who smoked excessively.

A small but consistent deficit of neurologic symptoms was noted among male parkinsonians who smoked, but not among the corresponding females, in the hospital survey (1). These findings were reversed in the present study, suggesting either that smoking does not substantially affect the neuropathologic course of Parkinson's disease or that considerably larger sample sizes would be necessary to demonstrate the effects with consistency. The latter explanation probably applies to the somewhat inconsistent findings on cigar and pipe smoking habits of parkinsonians as well.

The difficulties associated with defining the presence or absence of Parkinson's disease in individual patients have been alluded to above. One may assume that the diagnosis is made more validly and reliably by neurologists and neurosurgeons, and more variably by other physicians. If so, then the effects of misdiagnosis may be studied by comparing the characteristics of parkinsonians classified by the two groups of physicians, i.e. by the neurological and nonneurological panels.

When this was done in the present survey, relatively few salient differences emerged. Proportionally more males, more Negroes and younger individuals were referred by the neurological panel. Relatively more of the neurological panel patients were currently taking anti-Parkinson drugs excluding L-dopa and, perhaps obviously, more had undergone surgical intervention or were on L-dopa. The reported prevalence of most neurologic symptoms was somewhat higher among them. None of these differences between the panels were statistically significant. We may, therefore, conclude that in epidemiologic studies on etiologic factors in Parkinson's disease one may be justified in utilizing patients diagnosed by nonspecialists as well as by neurologists and neurosurgeons, should it prove difficult to attain statistically adequate sample sizes.

The present investigation also suggests one practical model for community surveys of chronic disease. (A more extensive treatment of the community as an epidemiologic laboratory has been published elsewhere (12)). Sampling physicians is logistically much simpler than sampling patients directly. It obviates the necessity to conduct physical examinations or, alternatively, to rely on the patients themselves for diagnosing the presence or absence of the disease of interest. It makes possible the study of patients in all diagnosed stages of the given condition, whether previously hospitalized or not. And, perhaps equally important, it coopts the practicing physician into collaborative basic research on the causes or concomitants of disease.

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